extended to Monday, September 23, 2002. If there is any deficiency or surplusage of the fees enclosed for the Extension of Time (fee), please obtain any such deficiency or credit the surplusage to Deposit Account 08-3255 and advise Applicants' Agent.

Applicant encloses herewith an Information Disclosure Statement (IDS) along with the prior art cited. If a fee is required with respect to the enclosed IDS, the Commissioner is authorized to access Applicant's Deposit Account No. 08-3255 for the required fee, and advise Applicant's Agent upon doing so.

IN THE ABSTRACT

No changes.

IN THE DISCLOSURE

No changes.

IN THE CLAIMS

Please amend the following claims.

1. (Amended) A process of making a solid pharmaceutical composition comprising moexipril magnesium, said process comprising the step of reacting moexipril or an acid addition salt thereof with an alkaline magnesium compound in the presence of a solvent so as to convert [most or all of] at least 70% of the moexipril or moexipril acid addition salt to moexipril magnesium.

5. (Twice Amended) The process of Claim 1 comprising the steps of:

i) adding the moexipril or acid addition salt thereof and the alkaline magnesium compound to solvent;

ii) using the resultant solution or suspension to wet granulate with[other] excipients to obtain a wet mass;

iii) drying the wet mass to obtain a dried mass; and

iv) further processing the dried mass into the solid pharmaceutical composition.

7. (Twice Amended) The process of Claim 1 comprising the steps of:

i) adding the moexipril or acid addition salt thereof to solvent;

ii) using the resultant solution or suspension to wet granulate a mixture of the alkaline magnesium compound and one or more [other] excipients to obtain wet mass;

iii) drying the wet mass to obtain a dried mass, and

iv) further processing the dried mass into the solid pharmaceutical composition.

8. (Twice Amended) The process of Claim 1 comprising the steps of:

i) mixing the moexipril or acid addition salt thereof and alkaline magnesium compound with one or more [other] excipients;

ii) adding a solvent and mixing to obtain a wet mass;

iii) drying the wet mass to obtain a dry mass; and

iv) further processing the dried mass into the solid pharmaceutical composition.

12. (Twice Amended) The process of any one of Claims 1, 2, 3, 5, 6, 7, or 8 wherein the percentage of the moexipril or acid addition salt converted to moexipril magnesium is [substantially] greater than [about] 80%.

13. (Twice Amended) The process of Claim 12 wherein the percentage of the moexipril or acid addition salt thereof converted to moexipril magnesium is [substantially] greater than 90%.

18. (Amended) The process of Claim 4 wherein the percentage of the moexipril or acid addition salt converted to moexipril magnesium is [substantially] greater than [about] 80%.

REMARKS

Claims 1, 5, 7, 8, 12, 13 and 18 now stand rejected under 35 U.S.C. 112, second paragraph, as being indefinite for failing to particularly point out and distinctly claim the subject matter which applicant regards as the invention.

The Examiner objects to the term "most" which allegedly renders the claim indefinite. The claims therefore have been amended to eliminate this term.

The Examiner also objects to the term "other" as allegedly indefinite, and the claims have been therefore amended. The Examiner also objects to the term "substantially" as a relative term, which renders the claim indefinite. This is a term used conventionally in claim drafting. The term is eliminated however with these amendments with no admission being made that it is in fact necessary to do so. The same is true for the Examiner's objection to the term "about". Full reconsideration is requested.

Claims 1 to 18 now stand rejected under 35 U.S.C. 103(a) as being unpatentable over Harris et al. (U.S. Patent No. 4,743,450) alone or in view of Hoefle et al. (U.S. Patent No. 4,344,949).

The essence of that which is taught and claimed in United States Patent No. 4,743,450 is an ACE inhibitor which is susceptible to cyclization, hydrolysis, and discoloration, and a suitable amount of an alkaline earth in the composition as a stabilizer. No where within the reference is there discussed any reactions but only combining of the active and the stabilizer. The reference is mute with regard to preparation of moexipril magnesium but only teaches contacting or combining the materials. For the composition to contain a stabilizer, clearly it must not have reacted with the drug, suitable saccharides or suitable excipients. Please refer to column 1 lines 15 to 40 for a discussion of the problem being solved and Harris' solution.

United States Patent No. 4,743,450 to Harris et al clearly teaches a process for making **stabilized** compositions comprising an ACE inhibitor such as enalapril, quinapril or indolapril. Example A refers to a wet granulation method for the

manufacture of tablets from the listed materials including quinapril hydrochloride and magnesium carbonate in the amounts indicated which are not reacted but combined. The Examiner is referred to column 1, line 51 wherein it states, that an amount of a stabilizer compound suitable to retard cyclization, hydrolysis, and/or discoloration is contained in the pharmaceutical composition and that the composition is formed by the steps of "contacting" the drug with an amount of stabilizer suitable to retard cyclization and/or hydrolysis. It is also stated at the bottom of that column that the composition will also contain substances which do not interfere with the function of the stabilizing additives.

Referring to column 3, at line 25 of United States Patent No. 4,743,450, the use of the stabilizers is discussed extensively and the manner in which the cyclization and hydrolytic instability of the composition can be stabilized using a suitable quantity, i.e. an effective amount of an alkaline stabilizer which is most preferably magnesium. The amount utilized is any amount which will effectively retard or prevent degradation of the ACE inhibitor components. Further at the same column, regarding the selection of saccharides which might be used, they are considered substances which do not contain groups which could significantly interfere with the function of either the metal containing component or the drug component. Further in relation to the excipients they are selected from those that do not interfere with the alkaline earth metal stabilizer's function in the composition. There is no discussion as to how much wetting material should be used, other than Example C, wherein an amount of purified water is indicated but no use for that water is further

discussed. Clearly therefore, it is impossible to conclude that United States Patent No. 4,743,450 discloses a process comprising the step of "reacting" since the magnesium compound must remain present in the final composition in order to fulfill its role as a stabilizer.

In Applicant's process sufficient water is introduced (as a solvent) in the process to moisten and to thereby permit a reaction to occur. There is no discussion or teaching in United States Patent No. 4,743,450 relating to this process. The Reference United States Patent No. 4,743,450 does not result in a solid pharmaceutical composition comprising moexipril magnesium. Respectfully, the Examiner is misreading References United States Patent No. 4,743,450 and reaching an incorrect conclusion.

Respectfully therefore, claim 1 and those depending there-from of the present application cannot be refused as being obvious in relation to Reference United States Patent No. 4,743,450 since clearly nowhere within is there taught,

> *"A process of making a solid pharmaceutical composition comprising moexipril magnesium, said process comprising the step of reacting moexipril or an acid addition salt thereof with an alkaline magnesium compound in the presence of a solvent so as to convert at least 70% of the moexipril or moexipril acid addition salt to moexipril magnesium."*

Respectfully, the Examiner has concluded that applicant's invention is obvious without pointing out any specific disclosure in the specification of United States Patent No. 4,743,450 which discuss the end result being moexipril magnesium.

The teachings of United States Patent No. 4,743,450 point in a different direction to including a stabilizer with the ACE inhibiter and therefore cannot render obvious Applicant's claims to those skilled in the art.

Should the Examiner allege; United States Patent No. 4,743,450 discloses the step of allegedly **"reacting"** quinapril hydrochloride with magnesium carbonate this would clearly be a misreading of the reference, as it teaches combining and contacting but in no way discusses reacting. It is clear from the teachings of United States Patent No. 4,743,450 that a reaction is not desirable since the saccharides and excipients, lubricants, and binders, are selected so as to not interfere with the stabilizing function of the stabilizer. Example A was discussed above and fails to anticipate or render obvious the claims for the reasons also set out above.

Clearly, a process of making a solid pharmaceutical composition comprising moexipril magnesium is taught by Applicant. United States Patent No. 4,743,450 does not teach such a process. Moexipril magnesium is only a result of Applicant's process which includes the step of **reacting** (emphasis added) moexipril or an acid addition salt thereof with an alkaline magnesium compound. To do so a solvent must be present in order for the reaction to occur, and the solvent must be present in an amount so as to convert the moexipril or moexipril acid addition salt to moexipril magnesium. This simply is not taught directly or indirectly in United States Patent No. 4,743,450 and further in any combinations thereof. There is no discussion whatsoever of moexipril magnesium as a solid pharmaceutical composition in any of

the references cited herein by the U.S. Examiner. Such a reaction is not disclosed, inferred, suggested or discussed. In fact only the stabilizing activity of the magnesium compound is discussed in Harris and the importance of avoiding excipients and saccharides which might interfere with that stabilizing function.

> *The traditional test enunciated in Graham vs. John Deere Company 383 U.S. 1, 148 U.S.P.Q. 459 1966, for Section 103 nonobviousness requires the fact finder to make several determinations. The test provides that the scope and content of the prior art be determined, the differences between the prior art and the claims at issue be ascertained, and the level of ordinary skill in the pertinent art be resolved. Thus, the patentability of the claims at hand must stem from the fact that the specific combination of the claimed elements was not disclosed in the prior art and the additional allegation that the specific combination of claimed elements was nonobvious to one of ordinary skill in the art.*

It is submitted that Applicant has clearly set out these differences above and full reconsideration is requested. The scope and content of Harris and Hoefle(following have been determined. Applicant therefore has amended the claims to more specifically define his invention to a process which limitation was not disclosed in Harris et al and Applicant's claims clearly identify over Harris since Harris does not disclose directly or indirectly or infer in any way :

> "A process of making a solid pharmaceutical composition comprising moexipril magnesium, said process comprising the step of reacting moexipril or an acid addition salt thereof with an alkaline magnesium compound in the presence of a solvent so as to convert at least 70% of the moexipril or moexipril acid addition salt to moexipril magnesium."

Clearly all claims depend from Claim 1. How therefore could they lack an inventive step if Claim 1 is in fact inventive which Applicant has correctly concluded and argued, in spite of the assertions of the Examiner. Claim 2 refers to the process of Claim 1 further comprising the steps of adding the moexipril or acid addition salt

thereof and the alkaline magnesium compound to the solvent and mixing in the liquid state and subsequently evaporating the solvent to obtain a dried material and further processing the dry material into a solid pharmaceutical composition. This further step dependent on Claim 1, the process for making moexipril magnesium, is based on the reaction of Claim 1 taking place in the liquid state. For the same reasons therefore set out in relation to Claim 1, Claim 2 would therefore be novel and non-obvious.

The same arguments could be put forward in relation to Claim 5 which relates to the process of Claim 1 for a process of making moexipril magnesium heretofore unknown comprising the further steps of preparing a wet granulation so that the reaction to form the moexipril magnesium takes place in the wet mass which is subsequently further dried and processed to form the solid pharmaceutical composition. Again for the same reasons in relation to the applied references in Applicant's arguments above, Claim 5 is novel and non-obvious to those skilled in the art.

Referring to Claim 6, the same arguments in relation to Claim 5 and Claim 1 would be true, as would further be true for Claim 7 and 8. The balance of the Claims represent specific limitations to the process of making moexipril magnesium which is heretofore unknown.

All the dependent claims are therefore inventive in view of the argument set out above since none of United States Patent No. 4,743,450 teaches the invention, moexipril magnesium.

Applicant herewith submits the Product Monograph for Univasc® (Moexipril Hydrochloride Tablets) wherein the tablets marketed by Schwarz Pharma (as listed in the FDA Orange Book as per the teachings of United States Patent No. 4,743,450) include magnesium oxide; unreacted but combined and functioning as a stabilizer (see first page). The Examiner is referred to those pages. Full reconsideration is respectfully requested.

Referring now to United States Patent No. 4,344,949 to Hoefle et al, clearly moexipril is taught along with other ACE -inhibitors. But there is no teaching of the problems of stabilizing the moexipril hydrochloride tablets as discussed in Harris and Gu, et al previously provided with Applicant's prior Information Disclosure Statement and discussed within Applicant's disclosure. Hoefle does not discuss the issue of stability whatsoever. However, Gu, et al does and it is further discussed, the importance of stabilizing the product in order to avoid cyclization processes and how the stability varied with the phvalues. For example, on page 381 at column 2, it was determined that with ph values below 4.5, a significant amount of degradation occurred. However at ph values between 4.5 and 10 the degradation rate was about 10 times slower. Gu also discusses that the stabilization is a result from the neutralization of the acid drug by basic excipients at the outer surface of the granulated material. However, primarily the product is moexipril hydrochloride as the active. This is consistent with the teachings of Harris. Hoefle, however does not even address the issues of stability but is merely a basic teaching with respect to the

pharmaceutical compositions useful as anti-hypertensive agents. Hoefle claims particular compounds such, as for example, that which is found in Claim 3. Nothing else might be inferred from the teachings of Hoefle and even if one were to read Harris in view of Hoefle, the resulting combination would not be more than, respectfully, merely the teachings of Harris. Even if, as per arguments suggested by the Examiner on page 3 of the Report of March 21, 2002, that Harris teaches the process for making a solid pharmaceutical composition in the forms of tablets using wet granulation comprising a method of stabilizing ACE-inhibitor drugs in combination with an alkaline agent (magnesium carbonate as the stabilizer), ... The Examiner states that Harris, et al is deficient in the sense that it does not expressively suggest the use of moexipril in their formulation. The Examiner states it would be obvious to use any of the various ACE-inhibitors available, including moexipril in combination with alkaline agents. This may be the case, but what would motivate one skilled in the art in reading Harris to carry out Applicant's process as follows.

> A process of making a solid pharmaceutical composition comprising moexipril magnesium, said process comprising the step of reacting moexipril or an acid addition salt thereof with an alkaline magnesium compound in the presence of a solvent so as to convert at least 70% of the moexipril or moexipril acid addition salt to moexipril magnesium.

There is no motivation to react the ACE-inhibitor with the alkaline agent but merely to combine it so that the alkaline agents can act as stabilizers as set out above.

Referring to the teachings of Hoefle, the Examiner asserts that the use of quinapril and moexipril are taught in United States Patent No. 4,344,949. Although this may be true, clearly there is no teachings of Applicant's invention as set out above and therefore there is nothing within the teachings of Harris and/or Hoefle that would motivate one skilled in the art to arrive at Applicant's claim set. Even if one skilled in the art were to combine Harris and Hoefle they would arrive at moexipril hydrochloride which is stabilized by an alkaline agent and preferably

magnesium oxide as per the product monograph of the moexipril hydrochloride tablets manufactured by Schwarz Pharma attached in the Information Disclosure Statement provided herewith. Applicant is not "combining" but is "reacting" the active and the agents to result in the moexipril magnesium.

In fact it is well established that for a combination of references to render an invention obvious, it must be obvious that the references can be combined; In Re Avery 186 U.S.P.Q.161 (CCPA 1975). The references themselves and not in retrospect, must suggest what has to be done. In Re: Skoll 187 USPQ 481 (CCPA 1975). There must be some reason for the combination other than hindsight gleaned from their invention itself. Interconnect Planning Corp., vs. Feil, 774 F. 2d 1132, 1134 (Fed. Cir. 1985). See also Panduit Corp. vs. Dennision Mfg. & Co., 810 F. 2d 1561, 1568 (Fed. Cir. 1988) where the court said:

> "Elements of separate prior art patents cannot be combined when there is no suggestion of such combination anywhere in those patents".

Although the Examiner suggests that the structure could readily be modified to form a combination of the claims at issue, the mere fact that the prior art could be so modified would not have made the modification obvious unless the prior art suggested the desirability of the modification. Please See in Re: Gordon 733 F. 2d 900-902, 221 USPQ 1125, 1127 (Fed. Cir. 1984); In Re: Grabiak, 769 F. 2d 729, 731, 226 USPQ 870, 872 (Fed. Cir. 1985).

Respectfully, the Examiner is creating a 20/20 hindsight reconstruction using Applicant's invention as a blue print to allegedly find elements of Applicant's combination in the prior art. This is not permissible as set out below.

In Re: Fritch, 23 U.S.P.Q. 2d 1780 (Fed. Cir. 1992)

> *"Wilson and Hendrix fail to suggest any motivation for, or desirability of, the changes espoused by the Examiner and endorsed by the Board. Here, the Examiner relied upon hindsight to arrive at the determination of obviousness. It is impermissible to use the claimed invention as an instruction manual or "template" to piece together the teachings of the prior art so that the claimed invention is rendered obvious. The court has previously stated that "[o]ne cannot use hindsight reconstruction to pick and choose among isolated disclosures in the prior art to deprecate the claimed invention."*

Clearly there is no motivation within Harris to modify his composition into Applicant's process absent some teaching in Harris to do so with or without the teachings of Hoefle, which is simply not the case.

ATD Corporation v. Lydall, Inc., 48 USPQ 2d 1321, 1329 (Fed. Cir. 1998)

> Determination of obviousness can not be based on the hindsight combination of components selectively culled from the prior art to fit the parameters of the patented invention. **There must be a teaching or suggestion within the prior art, or within the general knowledge of a person of ordinary skill in the field of the invention, to look to particular sources of information, to select particular elements, and to combine them in the way they were combined by the inventor.(emphasis added)**

In re Oetiker, 24 USPQ 2d 1443, 1446 (Fed. Cir. 1992)

> The combination of elements from non-analogous sources, in a manner that reconstructs the applicant's invention only with the benefit of hindsight, is insufficient to present a prima facie case of obviousness. **There must be some reason, suggestion, or motivation found in the prior art whereby a person of ordinary skill in the field of the invention would make the combination.** (emphasis added)That knowledge can not come from the applicant's invention itself.

Hindsight is not appropriate when considering the claim set of Applicant.

In Re: Rouffet, 47 U.S.P.Q. 2d 1453 (Fed. Cir. 1998)

> *"As this court has stated, "virtually all [inventions] are combinations of old elements." Environmental Designs, Ltd. v. Union Oil Co., 713 F.2d 693, 698, 218 USPQ 865, 870 (Fed. Cir. 1983); see also Richdel, Inc. v. Sunspool Corp., 714 F.2d 1573, 1579-80, 219 USPQ 8, 12 (Fed. Cir. 1983) ("Most, if not all, inventions are combinations and mostly of old elements."). Therefore an examiner may often find every element of a claimed invention in the prior art. If identification of each claimed element in the prior art were sufficient to negate patentability, very few patents would ever issue. Furthermore, rejecting patents solely by finding prior art corollaries for the claimed elements would permit an examiner to use the claimed invention itself as a blueprint for piecing together elements in the prior art to defeat the patentability of the claimed invention. Such an approach would be "an illogical and inappropriate process by which to determine patentability." Sensonics, Inc. v. Aerosonic Corp., 81 F.3d 1566, 1570, 38 USPQ 2d 1551, 1554 (Fed. Cir. 1996).*
>
> *To prevent the use of hindsight based on the invention to defeat patentability of the invention, **this court requires the examiner to show a motivation to combine the references that create the case of obviousness. In other words, the examiner must show reasons that the skilled artisan, confronted with the same problems as the***

inventor and with no knowledge of the claimed invention, would select the elements from the cited prior art references for combination in the manner claimed. (emphasis added)

This court has identified three possible sources for a motivation to combine references: the nature of the problem to be solved, the teachings of the prior art, and the knowledge of persons of ordinary skill in the art. In this case, the Board relied upon none of these. Rather, just as it relied on this high level of skill in the art to overcome the differences between the claimed invention and the selected elements in the references, it relied upon the high level of skill in the art to provide the necessary motivation. The Board did not, however, explain what specific understanding or technological principle within the knowledge of one of ordinary skill in the art would have suggested the combination. Instead, the Board merely invoked the high level of skill in the field of art. If such a rote invocation could suffice to supply a motivation to combine, the more sophisticated scientific fields would rarely, if ever, experience a patentable technical advance. Instead, in complex scientific fields, the Board could routinely identify the prior art elements in an application, invoke the lofty level of skill, and rest its case for rejection. To counter this potential weakness in the obviousness construct, the suggestion to combine requirement stands as a critical safeguard against hindsight analysis and rote application of the legal test for obviousness.

Because the Board did not explain the specific understanding or principle within the knowledge of a skilled artisan that would motivate one with no knowledge of Rouffet's invention to make the combination, ***this court infers that the examiner selected these references with the assistance of hindsight. This court forbids the use of hindsight in the selection of references that comprise the case of obviousness.*** (emphasis added)*See In re Gorman, 933 F.2d 982, 986, 18 USPQ 2d 1885, 1888 (Fed. Cir. 1991). Lacking a motivation to combine references, the Board did not show a proper prima facie case of obviousness. This court reverses the rejection over the combination of King, Rosen and Ruddy."*

Applicant further submits that a correct and recent statement of the law of obviousness is presented within Windsurfing International Inc. and Fred Ostermann GMBH et al, in the Re: Sernaker reasoning of the Court of Appeal 702 F.2d 989 (Federal Circuit 1983) when it was concluded that the following related test are appropriate standards against which to make an obviousness determination:

(a) whether a combination of the teachings of all or any of the references would have suggested (expressly or by implication) the possibility of achieving further improvement by combining such teachings along the line of the invention in suit, and

(b) whether the claimed invention achieved more than a combination which any or all of the prior art references suggested expressly or by reasonable implication.

Referring to the Windsurfing case, it was determined that although the test (a) was satisfied, the test (b) was not satisfied because the prior art references in combination do not make an invention obvious unless something in the prior art references would suggest the advantage to be derived from combining their teachings. It was therefore concluded that the patented invention in the Windsurfing case resulted in more than a combination suggested by any of the prior art references. Applicant